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09/995,007	11/26/2001	Nancy Carrasco	96700/708	9968

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Craig J. Arnold
Arnster, Rothstein & Ebenstein
90 Park Avenue
New York, NY 10016

EXAMINER	
SPIEGLER, ALEXANDER H	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,007	CARRASCO ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response to Applicants' response, filed on December 9, 2003. Currently, claims 56-86 are pending and are rejected. This action contains new rejections necessitated by Applicants' amendments. For example, Claim 56 has been amended to recite, "wherein the nucleic acid probe comprises nucleotides set forth in SEQ ID NO: 1 or wherein the nucleic acid probe detects nucleotides set forth in SEQ ID NO: 1", Claim 63 has been amended to recite, "with a protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208", and Claims 80-86 have been newly added and are rejected herein. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 56-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 56-62 are indefinite over "*nucleotides* set forth in" because it is not clear as to whether this means all of the nucleotides of SEQ ID NO: 1 (e.g., comprising the nucleic acid sequence of SEQ ID NO: 1) or some of the nucleotides of SEQ ID NO: 1 (e.g., a portion of SEQ ID NO: 1).

B) Claims 63-70 are indefinite over the recitation of "a protein comprising twelve

transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208" because it is not clear as to what "Asp 16, Glu 79 and Arg 208" refers to. That is, it is not clear where the numbering of these amino acid residues begins or what the reference point these residues are derived from.

C) Claims 80-86 are indefinite over the recitation of "the nucleotide sequence" because this recitation lacks antecedent basis.

Written Description

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 63-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are broadly drawn to a method for determining whether a mammalian sodium/iodide symporter is present in a sample, the method comprising contacting the sample with an antibody that is immunoreactive with the mammalian sodium/iodide symporter, wherein detecting binding of the antibody to the mammalian sodium/iodide symporter indicates that the mammalian sodium/iodide symporter is present in the sample, and wherein the antibody is

immunoreactive with *any* "protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208".

These claims encompass the genus of any antibody that is "immunoreactive" with *any* "protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208". Accordingly, this claim language would encompass a large number of possible antibodies "immunoreactive" with a large number of possible proteins "comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208".

The specification discloses the polypeptide of SEQ ID NO: 2.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention. The invention is, for purposes of the written description inquiry, *whatever is now claimed* (See page 1117)." (emphasis added)

In the instant case, the specification does not convey with reasonable clarity to those skilled in the art that, as of the filing date, that Applicants' were in possession of the broadly claimed invention. While the claims are drawn to some structural limitations (twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208), the specification only teaches one amino acid that appears to fit this genus, namely, SEQ ID NO: 2. Furthermore, it is noted that it is not clear where the numbering of these amino acid residues begins or what the reference point these residues are derived from. Accordingly, because the specification does not adequately describe the large genus encompassed by the claims (e.g., by a representative number of species), a person skilled in the art would not recognize that the inventor had possession of the claimed invention.

Enablement

6. Claims 56-86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a method of detecting a nucleic acid encoding a mammalian sodium/iodide symporter, the method comprising, providing a sample containing nucleic acid, contacting the sample with a probe comprising the nucleotide sequence of SEQ ID NO: 1 under hybridization conditions to form a complex between said probe and complementary target nucleic acids, and detecting the presence of said complex, wherein the detection is indicative of the presence of a nucleic acid encoding a mammalian sodium/iodide symporter; and 2) a method for determining whether a mammalian sodium/iodide symporter is present in a sample, the method comprising contacting the sample with an antibody that is immunoreactive with the mammalian sodium/iodide symporter, wherein detecting binding of the antibody to the mammalian sodium/iodide symporter indicates that the mammalian sodium/iodide symporter is present in the sample, and wherein the antibody is immunoreactive with a protein having the amino acid sequence set forth in SEQ ID NO: 2, does not reasonably provide enablement for 1) a method of determining whether a mammalian sodium/iodide symporter is expressed in a mammalian tissue, the method comprising contacting nucleic acid from the mammalian tissue with a nucleic acid probe, wherein detecting hybridization of the nucleic acid probe to the nucleotide sequence indicates that the mammalian sodium/iodide symporter is expressed in the mammalian tissue, and wherein the nucleic acid probe comprises *nucleotides* set forth in SEQ ID NO: 1 or wherein the nucleic acid probe detects *nucleotides* set forth in SEQ ID NO: 1; or 2) a method for determining whether a mammalian sodium/iodide symporter is present in a sample, the method comprising contacting the sample with an antibody that is immunoreactive with the

mammalian sodium/iodide symporter, wherein detecting binding of the antibody to the mammalian sodium/iodide symporter indicates that the mammalian sodium/iodide symporter is present in the sample, and wherein the antibody is immunoreactive with *any* "protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208", or 3) a method of determining whether a mammalian sodium/iodide symporter is expressed in a mammalian tissue, the method comprising contacting nucleic acid from the mammalian tissue with two or more nucleic acid probes, wherein detecting hybridization of the nucleic acid probes to the nucleotide sequence indicates that the mammalian sodium/iodide symporter is expressed in the mammalian tissue, and wherein each nucleic add probe comprises different or overlapping regions of nucleotides set forth in SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. In *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

Also, MPEP 2164.01 states:

"Even though the statute does not use the term 'undue experimentation,' it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)."

The *Wands* court outlined several factors to be considered in determining whether a disclosure would require undue experimentation:

"They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* at 1404.

In the instant case, the specification does not enable one of skill in the art to make and use the claimed invention for the following reasons:

(1) ***Nature of the Invention & Breadth of the Claims***

Claims 56-62 are drawn to detecting a whether a mammalian sodium/iodide symporter is expressed in a mammalian tissue by detecting the hybridization of a nucleic acid probe comprising "nucleotides" set forth in SEQ ID NO: 1 or a probe that "detects nucleotides" set forth in SEQ ID NO: 1. Thus, the claims are drawn to contacting nucleic acid from a mammalian tissue with *any* probe comprising "nucleotides" set forth in SEQ ID NO: 1 or *any* probe that "detects nucleotides" set forth in SEQ ID NO: 1.

The specification states, "The nucleic acid probes of the present invention may be DNA or RNA and may vary in length from about 8 nucleotides to the entire length of the mammalian sodium/iodide symporter." (page 11, lines, 34-37)

Thus, the claims are drawn to hybridizing a nucleic acid probe of as little as 8 nucleotides (or less, since the term "about" is used) to nucleic acid from a mammalian tissue, wherein the hybridization of these 8 nucleotides (or less) indicates the expression of the mammalian sodium/iodide symporter.

Claims 63-70 are drawn to a method of contacting a sample with any antibody that is "immunoreactive" with *any* "protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208". This encompasses contacting any of a large number of possible antibodies "immunoreactive" with a large number of possible proteins "comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208" for determining whether a mammalian sodium/iodide symporter is present.

Claims 80-86 are drawn to contacting nucleic acid from the mammalian tissue with two or more nucleic acid probes (of 8 nucleotides or less, see above), wherein detecting hybridization of the nucleic acid probes to the nucleotide sequence indicates that the mammalian sodium/iodide symporter is expressed in the mammalian tissue, and wherein each nucleic add probe comprises different or overlapping regions of nucleotides set forth in SEQ ID NO: 1. These regions could be 8 nucleotides (or less) of a different nucleic acid sequence or the same (e.g., overlapping) nucleic acid sequences. Again, the claims are drawn to hybridizing a nucleic acid probe of as little as 8 nucleotides (or less) to nucleic acid from a mammalian tissue, wherein

the hybridization of these 8 nucleotides (or less) indicates the expression of the mammalian sodium/iodide symporter.

(2) ***Relative Skill of those in the Art, State of the Prior Art, Amount of Direction or Guidance Presented & Presence or Absence of Working Examples***

The relative level of skill in molecular biology is high. This is evidenced by the lack of cloning or characterization of the cDNA encoding the mammalian sodium/iodide symporter prior to the present invention. (see specification, page 4, lines, 3-5) Therefore, the prior art is silent as to any nucleic acid probes of 8 nucleotides (or less), or any antibodies that are "immunoreactive" with *any* "protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208", that when hybridized to mammalian nucleic acid (or, in the case of antibodies, when bound to the sodium/iodide symporter), indicates mammalian sodium/iodide symporter expression.

The specification provides guidance through working examples of the isolation and characterization of the primary sequence and predicted secondary structure of the sodium/iodide symporter molecule. (see pages 17-22) The specification teaches the amino acid sequence of the mammalian sodium/iodide symporter (see SEQ ID NO: 2).

mammalian sodium/iodide symporter. Specifically, the specification does not teach what modifications can be made to a nucleic acid probe that could still function for detection mammalian sodium/iodide symporter expression.mammalian sodium/iodide symporter. Furthermore, the specification does not provide any examples of possible probes that when hybridized to mammalian nucleic acid; demonstrate the expression of the mammalian sodium/iodide symporter. any antibodies that are "immunoreactive" with *any* "protein

comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208", wherein detecting binding of the antibody to the mammalian sodium/iodide symporter indicates that the mammalian sodium/iodide symporter is present in the sample. Specifically, the specification does not teach what modifications can be made to specific residues or domains that could still function for detection mammalian sodium/iodide symporter expression.mammalian sodium/iodide symporter. Furthermore, the specification does not provide any examples of possible antibodies that are "immunoreactive" with *any* "protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208" that when contacted to the mammalian sodium/iodide symporter; demonstrate the presence of the mammalian sodium/iodide symporter.(3) ***Quantity of Experimentation Necessary & the Unpredictability of the Art***

In order to practice the invention, the practitioner must hybridize a probe of 8 nucleotides (or less) to the nucleic acid of a mammalian tissue, and then test the hybridization product to determine whether the mammalian sodium/iodide symporter was expressed. This experimentation would be completely driven by a trial and error process with no guidance from either the specification or the art as to which nucleotides are necessary, which modifications, if any, can be made for the probe, etc. Because such experimentation requires an extremely large amount of trial and error analysis, with little to no starting point, and because the skilled artisan must supply novel experimentation of first finding and then correlating possible probes with the expression of the mammalian sodium/iodide symporter, such analysis is unpredictable, and is therefore considered undue.

With respect to Claims 63-70, in order to practice the invention, the practitioner must first experiment to find antibodies that are "immunoreactive" with *any* "protein comprising twelve transmembrane domains and amino acid residues Asp 16, Glu 79 and Arg 208". Then, the practitioner would have to test these antibodies by contacting said antibodies to the mammalian sodium/iodide symporter, and determine whether the mammalian sodium/iodide symporter is present. This experimentation would be completely driven by a trial and error process with no guidance from either the specification or the art as to which amino acid residues are necessary, which modifications, if any, can be made for the antibody, etc. Because such experimentation requires an extremely large amount of trial and error analysis, with little to no starting point, and because the skilled artisan must supply novel experimentation of first finding and then correlating possible antibodies with the presences of the mammalian sodium/iodide symporter, such analysis is unpredictable, and is therefore considered undue.

Additionally, there is a high level of unpredictability because there are no previous experiments in the prior art that have taught the cloning or characterization of the cDNA encoding the mammalian sodium/iodide symporter prior to the present invention.

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

Applicants are reminded that the enablement requirement of 35 U.S.C. 112, first paragraph, is separate and distinct from the description requirement. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116-17 (Fed. Cir. 1991).

Conclusion

7. No Claims are allowable.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alexander H. Spiegler
March 18, 2004

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
3/18/04